EXHIBIT F

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON DIVISION

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	**Master File No. 2:12-MD-02327** **MDL 2327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**
THIS DOCUMENT RELATES TO: *Wave 6 Cases*	

EXPERT REPORT OF JOHN R. WAGNER, M.D.

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Gynecare Gynemesh PS, Prolift and Prolift +M

I have prepared this Expert Report in the matter of In re: Ethicon, Inc. Pelvic Repair System Products Liability Litigation, MDL No. 2327, currently pending in the United States District Court for the Southern District of West Virginia, before the Hon. Joseph R. Goodwin.

I. QUALIFICATIONS AND EXPERIENCE

A *curriculum vitae* providing the details of my education, experience and training is accompanies this report.

I am originally from St. Louis, MO. I attended Georgetown University for my undergraduate education, where I received a Bachelor of Arts degree in Political Science in 1983. I attended medical school at Mount Sinai School of Medicine, in New York and graduated in 1987.

I completed my internship and residency from 1987-1991 at University Hospital at Stony Brook. I was the Chief Resident in 1991. In my residency, I was trained in multiple urogynecologic procedures. I trained under Jim Droesch at University Hospital Stony Brook from 1987 to 1991. During that time, he initiated the Department of Surgical Gynecology which was a large surgical referral service for benign gynecologic conditions. We performed our own urodynamic studies and cystoscopies on an out-patient basis. I performed many surgeries for incontinence including Kelly plications, needle suspension procedures (such as the Stamey and Pereyra operations), Burch procedures, MMK's, and autologus vaginal slings. I performed many pelvic support procedures including paravaginal repairs as well as traditional bladder

suspensions. We performed multiple vaginal and abdominal operations for apical vaginal prolapse. These included sacrocolpopexy, multiple different types of culodoplasties, sacrospinous fixation, and high uterosacral ligament suspension.

At the time I worked at Stony Brook, there were very few national fellowships available in either minimally invasive surgery or urogynecology. Urogynecology is now recognized subspecialty, and I took and passed my Female Pelvic Medicine and Reconstructive Surgery boards in 2014. I have been Board Certified in OB/GYN since 1993.

For the past 25 years, I have worked in the same private practice, now called WGM Obstetrics & Gynecology. While I do practice obstetrics, my primary focus is surgical gynecology for benign conditions. Approximately half of the operations I perform are related to a minimally invasive surgical approach for large pelvic pathology. The other half is primarily related to pelvic prolapse and/or incontinence surgery. I am one of the few surgeons nationwide that utilizes a robotic single site approach to treat pelvic organ prolapse. I routinely perform robotic single site sacrocolpopexies and vaginal and/or uterine suspension procedures. I have a large volume of patients who suffer from stress incontinence and urge incontinence. I perform my own urodynamic studies in the office. My typical incontinence procedures utilize suburethral slings.

As regards teaching positions, I am currently a Clinical Associate Professor at Hofstra University School of Medicine. I serve as a co-director for the Department of Minimally Invasive Gynecology at Huntington Hospital. I am currently employed as an “at large educator” by three different university hospitals. There are currently four different OB/GYN residencies on Long Island. Three of these also have fellowship programs in minimally invasive gynecology

and/or urogynecology. I am currently actively involved in the teaching of senior residents and fellows from all of these programs.

The residents and fellows that I operate with are exposed to vaginal mesh repairs, abdominal mesh repairs and various forms of suburethral slings. The slings I utilize are primarily those made by Johnson & Johnson (and included the TVT-Exact, TVT Abbrevo, and TVT-O). I also performed the "Classic" TVT Retropubic for many years, and used TVT Secur extensively while it was on the market.

I routinely use the IFU's as part of my resident education as the IFU provides an excellent review of the product, its use, potential complications and warnings. I encourage my residents, when they are first exposed to these products, to take the IFU's home with them and to review them thoroughly.

When I first started in private practice, I performed Burch procedures on a regular basis. My two primary incontinence procedures were the Burch and the Pereyra needle suspension procedure. The Pereyra was less invasive, but had a significantly higher long term failure rate. The Burch procedure was more invasive but had a better long term result. Typically, a Burch procedure would require a 3-7day hospitalization and prolonged catheterization.

When the TVT became available, it revolutionized the treatment of stress incontinence. TVT provided long term outcomes equivalent to or better than the Burch procedure combined with a minimally invasive approach that was consistent with the needle suspension procedures. The landscape for treating stress incontinence was literally changed almost overnight. The

suburethral slings have so changed the treatment of SUI that there are urogynecologic fellows in today's world who graduate without ever seeing a Burch procedure.

From about 2000 to 2006, I used TVT Retropubic slings and estimate that I performed 600-800 procedures with that device. I then started using the TVT Secur device and continued to use that until 2012 when Ethicon discontinued it. I estimate that I performed approximately 800-1000 procedures to implant TVT Secur. Since the discontinuation of TVT Secur, I have primarily used TVT Abbrevo and TVT Exact to treat SUI. I perform approximately 6-8 TVT Abbrevo procedures per month since 2012 and approximately two per month with TVT Exact. TVT Exact is my sling of choice when a patient has intrinsic sphincter deficiency or has recurrent SUI following a prior sling.

I also have extensive experience in using Ethicon's mesh to treat prolapse, including Gynemesh PS, Prolift, Prolift +M and Prosima. I have been doing vaginal mesh prolapse repairs since approximately 2005. Initially, I began creating Gynemesh PS mesh "patches" to bolster my traditional vaginal repairs. This work was presented at a national ACOG meeting in 2006 as part of an award-winning presentation. The concept of augmenting vaginal repairs with mesh gained traction in the years after 2000 primarily because of two concurrent factors. The first was a general frustration with traditional native tissue repairs due to the high failure rate of these repairs even in the hands of experienced surgeons. The risk for reoperation following traditional suture repair is estimated to be 30-50%. (Withagen M. 2011; Altman 2011; Nieminen 2010; Jia 2008). The second factor was the evolution in the treatment of anterior abdominal wall hernias. General surgeons were gradually moving from more traditional repairs to mesh augmented repairs, primarily to reduce the recurrence risk following primary repair. The general surgical

literature was supporting not only the safety but the efficacy of these repairs compared to a more traditional approach. In the 1990s, various thought leaders in gynecologic surgery began proposing the use of mesh augmentation to minimize the risk of surgical failure and/or recurrence following prolapse repair. In 2002, Gynemesh PS received FDA clearance for use in prolapse repair. As a result, I began using the Gynemesh PS to augment my native tissue repairs. I hand cut patches to appropriately fit in the patient's anterior, apical or posterior compartments. These meshes were then sutured in place following a more traditional repair. When the Prolift system was introduced, I was trained on the device in December 2005. I immediately began using the Prolift system as my primary procedure for vaginal mesh repairs, and I completely abandoned the use of my hand cut patches.

The Prolift system utilized a similar large pore polypropylene mesh to the Gynemesh PS, and the repair itself was less invasive. It required less dissection and could be performed without the need for concomitant hysterectomy. In addition, Prolift provided an opportunity to perform an enterocele repair with mesh augmentation thereby improving the apical support to the posterior vagina compared to traditional enterocele repairs. Most importantly, the use of trocars was revolutionary. It facilitated placement of the mesh with minimal trauma to surrounding tissue. In addition, it allowed for dynamic tensioning of the mesh with the vagina in its normal anatomic position. This greatly facilitated placing the mesh on an appropriate level of tension thus minimizing the chance that the mesh itself would distort the vagina. Finally, I preferred the Prolift system to other similar products on the market. The trocars were comfortable, ergonomic, and smaller than other trocars such as the IVS tunneler. Smaller trocars translated into better tactile feedback when passing the trocar, less postoperative pain, and fewer potential complications.

When Prolift+M was introduced, I also incorporated this into my practice. I found that the Prolift+M was clinically very similar to the traditional Prolift. I liked the idea that the mesh was also partially absorbable. I estimate that I have implanted Prolift and Prolift +M in approximately 800-1000 patients (approximately 1-5 per week), and Prosima in about 20-30 patients.

Based on Ethicon's documentation, I received Ethicon-sponsored training to use the following devices: Prolift in December 2005 and June 2009, TVT Secur in September 2006, Prosima and TVTO in March 2010, and TVT Abbrevo in October 2010.

I served as a surgical proctor and preceptor for Ethicon from 2000 into 2011. This teaching primarily occurred at my hospital (Huntington Hospital). On occasion, I would travel to other hospitals to teach or proctor surgeons. I also served as a preceptor for TVT courses for Ethicon including a cadaver course that took place in Baltimore. As with my residents and fellows, when proctoring, I commonly utilized the IFU for educational purposes. During my time as preceptor, I believed that Ethicon reimbursed me a total of approximately $50,000.

II. MATERIALS REVIEWED

In the course of preparing this report, I have reviewed the published peer-reviewed medical literature on Gynecare Gynemesh PS, Prolift and Prolift +M, and more generally, the use of transvaginal mesh and other surgical procedures to treat prolapse. I have reviewed materials produced by Ethicon, including the Gynemesh PS, Prolift and Prolift +M Instructions for Use (IFU), patient brochures and professional education materials including the Prolift Surgeon's Resource Monograph, and Prolift Surgical Technique Guide. I have also read the publicly available materials issued by medical societies and the Food and Drug Administration

(FDA) regarding the use of transvaginal mesh to treat prolapse. A complete list of the materials that I have reviewed is provided with this Report, and will be supplemented as I review more materials.

III. PROLAPSE

Pelvic organ prolapse is a common condition in women. Pelvic organ prolapse (POP) is common, affecting as many as 50% of women who have had children. (Maher Cochrane Review 2016). Approximately 13% of all women will undergo surgery for pelvic organ prolapse. (ACOG-AUGS Practice Bulletin No. 176 (April 2017). There are various manifestations of pelvic organ prolapse, but they all represent some type of vaginal wall defect and/or hernias. When sections of the vaginal wall weaken, the adjacent organ can bulge into the vagina creating one of these hernias.

There are five different hernias that can occur in the vaginal wall. In the anterior vaginal wall, a weakness can occur beneath the urethra or the bladder. When the defect occurs beneath the urethra, it is referred to as a urethrocele. Typically, a urethrocele will be associated with stress incontinence. When the defect occurs beneath the bladder, it is a referred to as a cystocele. Cystoceles can also cause significant urinary dysfunction. When the vaginal wall weakens at the apex, this results in prolapse of the uterus. In the posterior vaginal wall, a weakness can develop in the region overlying the rectum. This allows the rectum to bulge into the vagina creating a rectocele. When the superior portion of the posterior vaginal wall weakens, a bowel hernia can develop. This is referred to as an enterocele. All of these hernias can occur individually or in

combination with each other. The symptoms experienced by the patient often depend on which hernia or combination of hernias is present.

IV. IMPACT OF PROLAPSE ON PATIENT QUALITY OF LIFE

Prolapse can be a very difficult and embarrassing for the patients who suffer from it, particularly more severe forms of prolapse.

While pelvic organ prolapse is not life-threatening, it can be extremely distressing to the patient. Common symptoms include a vaginal bulge and pressure. This bulge can be extremely uncomfortable. In addition, prolapse is often associated with voiding dysfunction including stress incontinence, urgency incontinence and chronic urinary tract infections. Defecatory dysfunction, including chronic constipation and anal incontinence, is also quite common. All of these complications can lead to significant physical and emotion distress. Prolapse can be extremely disabling and can adversely affect a patient's life and her ability to perform normal daily activities.

Pelvic organ prolapse can also have a significant negative impact on a patient's self-image. The anatomic distortion associated with the pelvic organ prolapse can lead to sexual dysfunction and dyspareunia. In addition, the urinary incontinence and anal incontinence associated with pelvic prolapse often makes it difficult for a patient to stay clean resulting in a sense of constant embarrassment and a loss of dignity. This can have a significant impact a patient's quality of life, particularly in their intimate relationships with their spouses and partners.

The negative impact of prolapse is perhaps most apparent in the postoperative period, after the patient has been treated. As a physician, it is most striking and rewarding to see the

expression of joyful relief on the face of patients after surgery. This sense of relief provides an excellent barometer to measure the longstanding negative impact that this disease has on patients. It is probably the best indicator of how this condition can negatively impact one's life both physically and emotionally.

V. DIAGNOSIS AND MEASUREMENT OF PROLAPSE.

The diagnosis of prolapse is based on visual inspection of the vagina at the time of a pelvic examination. The physician notes the presence of any vaginal hernia and the extent of that hernia. The accepted standardized technique for describing the presence and extent of pelvic organ prolapse is the POPQ scoring system. This system was introduced in 2010, revised in 2016 and is endorsed by the ICS (International Continence Society) and the IUGA (International Urogynecology Association). It basically divides the vagina into an upper area (near the uterus), a middle area, and a lower area (near the vaginal opening). The anterior vaginal wall and the posterior vaginal wall are then assessed in each of these regions. Any defect or hernia is recorded as it relates the hymenal ring. Measurements are done in centimeters. A defect that is present in the vagina is measured in negative numbers. A defect that projects beyond the hymenal ring is measured in positive numbers. In addition, the system also evaluates the vaginal opening, the size of the perineal body and the total vaginal length.

The POPQ system is a reliable and reproducible way to evaluate pelvic prolapse. It has good interobserver correlation. It allows objective assessments to be made of the extensive pelvic prolapse both before and after surgical correction. This improves the reliability and accuracy of various reports describing the success rates associated with pelvic organ prolapse repair. It

assures that all doctors are "speaking the same language" when they describe the presence and extent of various pelvic floor defects.

A simpler staging system, called the Baden-Walker system, can be employed to address isolated uterine prolapse. In this system, four stages are present. Stage II uterine prolapse reflects descent of the cervix to within 1 cm on either side of the hymenal ring. Stage I uterine prolapse would reflect prolapse higher in the vagina. Stage III uterine prolapse would reflect prolapse beyond the hymenal ring. Stage IV would be complete vaginal vault aversion with total uterine prolapse. This staging system is older, less complete, but still acceptable for describing pure uterine prolapse.

VI. TREATMENT OF PROLAPSE.

Treatment options for pelvic prolapse include expectant management, pessary placement or surgical correction.

Expectant management is a reasonable option for this condition due to the fact that is not life threatening. If the prolapse is mild, not uncomfortable to the patient, and not causing significant functional disorders, the problem can be managed with supportive care and reassurance. Occasionally, mild prolapse can be managed with topical estrogen therapy to make the vaginal skin less irritable and therefore less uncomfortable. In addition, certain conditions such as stress incontinence can be managed with pelvic floor muscle exercises. Bladder dysfunction can be managed with bladder training and pelvic floor muscle exercises. Defecatory dysfunction can also be managed with certain supportive care measures.

If expectant management with supportive care is not effective, then other options are available. Pessary placement represents the only non-surgical alternative. Pessaries are plastic

devices of various shapes and sizes that can be placed in the vagina to essentially "hold back" the prolapse. Some patients can be managed successfully with pessary therapy for many years. However, problems with pessary therapy include a chronic discharge and odor. In addition, the pessary itself can lead to pelvic discomfort and voiding or defecatory dysfunction. Long term pessary therapy can lead to vaginal erosion and bleeding. Furthermore, the pessary itself needs to be removed and cleaned on a regular basis. This can sometimes be accomplished by the patient herself; however, in most cases, multiple regular physician visits are required to remove, clean, and replace a pessary. Pessary treatment can also have a significant negative impact on a patient's sexual function.

Surgical therapy is appropriate for patients who have failed or declined conservative measures and pessary treatment. Surgical treatments can be divided into those that are performed abdominally and those are performed vaginally. In addition, surgical treatments can be divided into those that employ permanent mesh implants and those that do not. Surgical treatments that do not involve mesh implants include native tissue suture repairs. Biologic patches can also be employed to help bolster the repair. Mesh augmentations can be accomplished vaginally or abdominally. In addition, non-mesh operations can also be performed vaginally or abdominally.

Historically, all operations to correct pelvic organ prolapse involve native tissue suture repairs. The biggest complication of these traditional surgical repairs is the high risk for failure or recurrence. As a result, mesh augmentation has been employed as a means to lower that risk. In recent years, minimally invasive laparoscopic and robotic approaches have been developed to help aid in the abdominal mesh repairs of pelvic prolapse.

VII. THE DEVELOPMENT OF GYNECARE PROLIFT.

In June of 2000, a group of nine pelvic floor surgeons in France (the "TVM group") sought to develop a procedure using a transvaginal mesh which would be more uniform in approach than existing methods to implant mesh to treat prolapse. They selected as their implant a shaped form of Gynemesh PS. Gynemesh PS is a low-weight (44 g/m^2) Amid type 1 polypropylene mesh. (Jones et al., Tensile properties of commonly used prolapse meshes, Int. Urogyn. J. 2009; 20:847-53). The surgeons honed the procedure over a 5-year period and several hundred surgeries. The group assessed implant shapes and sizes, material composition, incisions, dissection techniques and implant fixation points. (Berrocal et al. (2004); Cosson, M., ICS Abstract (2005)).

The Gynecare Prolift kit evolved from the clinical experience and learnings of these sugeons. It includes a non-absorbable implant made of Gynemesh PS which comes in three pre-cut versions. The procedure can be performed in whole, as with a total kit, or in part with anterior or posterior only implants based on the surgeon's judgment and patient anatomy. The anterior part is implanted between the bladder and the vagina and is secured through the obturator foramen by two sets of arms. The posterior part is implanted between the rectum and the vagina and is secured by one arm passing through each ischiorectal fossa and sacrospinous ligament. The intermediate section corresponds to the vaginal apex and can be used in post hysterectomy patients or cut out to accommodate patients who seek to retain the uterus.

Cannula-equipped guides were used to optimize the passage of the mesh through the tissues, minimizing trauma to the tissue and arcus tendinous fascia pelvis (ATFP). The cannulas also permitted placement of the retrieval device. Retrieval devices would pass each prosthesis

strap through the pelvis. In most cases a hysterectomy could be avoided. (Fatton et al. 2007). The procedure could be performed on women with all stages of prolapse but was best suited for those with more advanced stages of prolapse. (Prolift Surgeon's Resource Monograph, pg. 3).

If a simultaneous hysterectomy is desired, a separate incision is recommended for the anterior Prolift and hysterectomy with the hysterectomy site closed horizontally and the Prolift site closed vertically. For optimal healing, they should not intersect (T incision). After the procedure, an anti-incontinence procedure (ie. midurethral sling) can be performed as well as perineorrhaphy. A foley catheter and lubricated vaginal packing is put into the vagina for 24 to 48 hours. The Prolift Surgical Technique Guide (2005) provides a detailed description for the surgeon on proper mesh placement in multiple scenarios.

The introduction of Prolift was a tremendous advance in the treatment of pelvic organ prolapse. The shape of the mesh was designed to mimic the natural vaginal supports. This decreased the normal variation among surgeons and helped to standardize the use of mesh to augment vaginal prolapse repairs. Prolift could also be performed without the need for a hysterectomy. This significantly decreased the morbidity of prolapse surgery and was an advantage over other abdominal and vaginal procedures.

As mentioned above, the use of trocars to place the mesh was a truly revolutionary idea. It allowed placement of mesh with less dissection and less trauma to the local vaginal tissues. More importantly, having the mesh arms housed in the trocar cannulas allowed the surgeon to dynamically set the tension of the mesh under direct visualization with the vagina in its normal anatomical position. This reduced the risk of over tightening or asymmetrical tightening of the mesh -- both of which could lead to distortion of the vagina. This was a tremendous advantage

of Prolift. No traditional vaginal or abdominal mesh procedure allowed the surgeon the opportunity to adjust the mesh under direct visualization after it was placed.

The Prolift system was composed of two parts -- an anterior implant and a posterior implant. The anterior portion was essentially a hammock designed to support the bladder. The hammock had four arms --- two on each side --- that held it in place. The arms went through the arcuate tendinious fascia (ATF) on each side and exited the pelvis via the obturator foramen. The apical portion of the mesh was attached to the cervix with sutures. The procedure began with careful dissection of the bladder off the vaginal epithelium. Trocars were then placed from the outside in through the obturator foramen, the ATF, and into the para-vaginal tissues bilaterally. The superior trocar penetrated the ATF near the ischial spine. The inferior trocar penetrated the ATF in the retro-public region near its insertion into the back of the pubic bone. The trocars were then removed and the cannulas were left in place. Mesh retrieval devices were then placed through each cannula and used to pull each mesh arm into its corresponding cannula. The cannulas containing the mesh arms were then left in place until the entire implant was secured. Then the vagina was returned to its normal anatomical position and the mesh arms were loosened and/or tightened under direct visualization to ensure that the mesh lay appropriately in the anterior compartment. Only then were the cannulas removed.

The posterior portion was a strip of mesh designed to lay against the posterior vaginal wall. There were two apical mesh arms that supported the implant. The apical region was sutured to the posterior cervix and the inferior region was sutured to the perineal body. The apical arms supported the implant, exited the pelvis through the sacrospinous ligament, and traveled through the ischioanal fossa. Dissection began in the posterior vaginal wall and the vagina was dissected off the rectum. The retroperitoneal space was explored and the

sacrospinous ligament was identified bilaterally. Trocars were placed through the ischioanal fossa bilaterally and up through each sacrospinous ligament to enter the para-vaginal space. Mesh retrieval devices were then placed through each cannula and used to pull each mesh arm into its corresponding sheath. Final adjustments of the mesh implant were then made with the vagina in its normal anatomical position before removing the trocar sheaths. If an anterior and posterior implant were both used, then the final tensioning would not be done until both implants had been placed.

Surgical principles during Prolift training and in the Prolift Surgical Technique Guide also stressed techniques for minimizing mesh erosions. Recommendations included making the vaginal incisions as small as possible. This was facilitated by the use of trocars to place the mesh as less dissection was necessary. In addition it was stressed that, if a hysterectomy was performed, a "T" incision at the vaginal apex was to be avoided, as this significantly increased the risk of mesh erosion in that area. Most importantly, surgeons were recommended to perform a full thickness dissection of the vaginal walls with care taken to leave the fibromuscular tissue layer attached to the vaginal epithelium. This was accomplished with the use of hydrodissection. Distention of the vaginal wall with fluid allowed identification of the fibromuscular tissue supporting the vaginal wall and facilitated leaving that layer intact and attached to the vaginal skin. Full thickness dissection is still considered an integral part of vaginal mesh repairs and a primary means of helping to prevent mesh erosions.

VIII. OTHER SURGICAL OPTIONS TO TREAT PROLAPSE

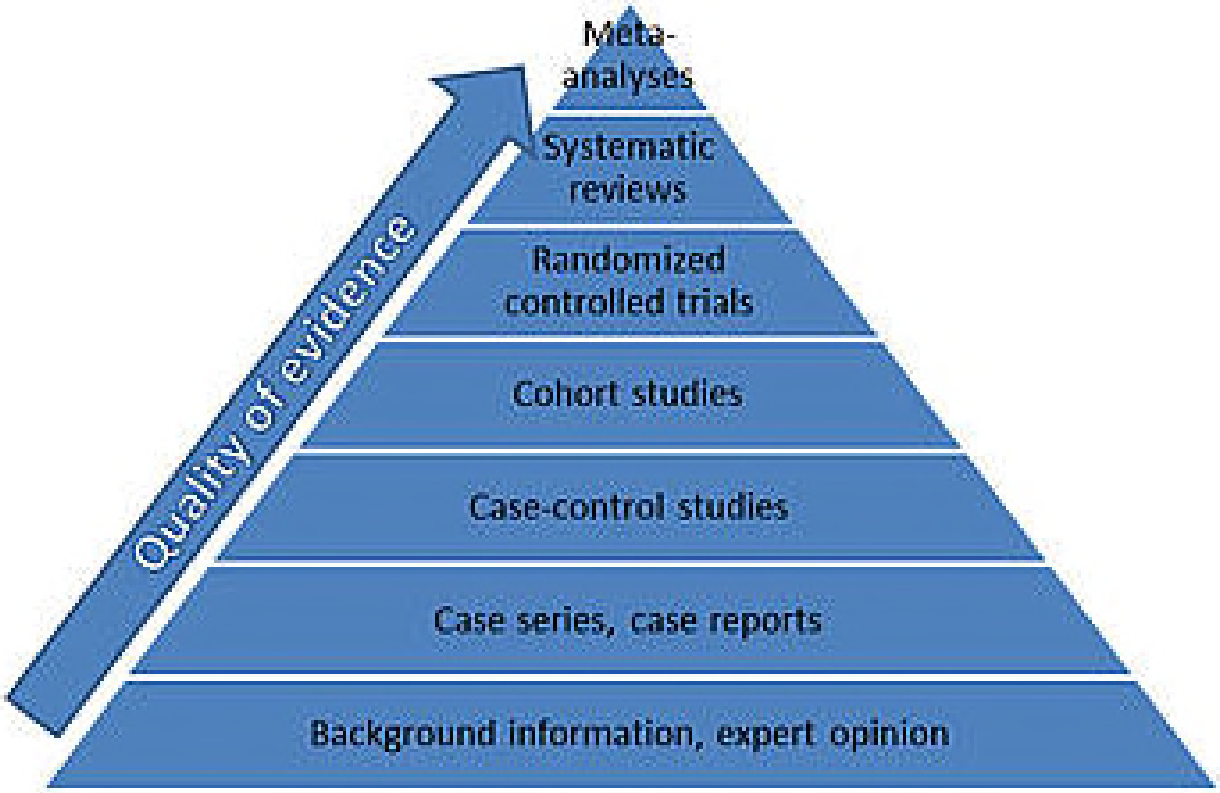
The introduction of Prolift was a significant advance in the surgical treatment of pelvic organ prolapse for a number of reasons. It provided surgeons with a minimally invasive transvaginal option for performing mesh augmented repairs of pelvic organ prolapse.

Abdominal operations to repair pelvic organ prolapse, such as sacral colpopexy, have long been associated with a higher morbidity compared to vaginal procedures. Abdominal surgery is associated with pulmonary, bowel and thromboembolic complications, as well as others. This increased morbidity continues to persist despite the fact that many of these abdominal procedures are now performed using minimally invasive laparoscopic or robotic techniques. Despite the increased morbidity, abdominal procedures achieve greater durability than native tissue repairs. By utilizing a mesh implant in a transvaginal approach, the Prolift procedure was designed to replicate the durability of the abdominal procedures while reducing the risk of complications associated with abdominal surgery. In addition, sacrocolpopexy often necessitates a hysterectomy. The further increases the morbidity associated with the prolapse repair. Prolift allowed for placement of vaginal mesh without the concomitant need for hysterectomy.

IX. MEDICAL LITERATURE ADDRESSING THE USE OF GYNECARE PROLIFT.

In evaluating the medical literature evaluating the performance of the Gynemesh PS, Prolift and Prolift +M products, I have utilized the Oxford Pyramid of Evidence, picture below, to assess the weight of the evidence and data that is described. Specifically, meta-analyses and systematic reviews of studies, and randomized controlled trials, and deemed among the most

reliable and credible forms of studies because of the volume of patient they assess and/or the quality of their methodology. These are followed by prospective or retrospective cohort studies which in general can provide very good information on a device's safety and effectiveness. Towards the bottom of the pyramid are case reports and case series which typically focus on particular complications or notable results that the investigator has observed in a relatively small number of patients. While these reports can be informative and play a role in informing surgeons about infrequently occurring events, they do not provide evidence with the level of reliability as the higher levels of studies, for one reason because they typically do not assess the complications against a denominator of patients who have received the device. This pyramid provides an important general framework within which to assess published data, but of course, specific studies need to be assessed individually for the quality of their methodology and reliability of their conclusions.



Not appearing at all on this pyramid are internal company emails and other product development documentation, on which many of the plaintiffs' experts rely so heavily. While internal company information and testing is informative, particularly as to the historical development of the device, the best assessment of the safety and effectiveness of transvaginal mesh products are the published studies assessing the *actual performance* of these products in women who are followed over a period of time. That is why the clinical studies are such an important basis of my opinions.

Since the introduction of Gynemesh PS in 2002, surgeons have conducted studies on these products and have published their findings in publicly-available medical journals throughout the world. These studies provide important information regarding not only the

effectiveness of these procedures, but also the nature, incidence, frequency and severity of potential complications. The publication of this information significantly contributes to the body of common knowledge that is possessed by trained pelvic floor surgeons. The most reputable of those journals, including many of those cited in this report and on my materials list, employ a rigorous peer review process to ensure the high quality and accuracy of the study's methodology, data analysis and reporting.

The medical literature on Prolift, which includes Level 1 evidence such as randomized controlled trials, shows that it provides significant benefit to well-selected patients, with a reasonable risk profile, when used by surgeons who are experienced with the device.

Fatton et al. (including authors among the nine French surgeons) performed a retrospective study of 110 Prolift patients with stage 3 or 4 prolapse. At 3 month follow up, the failure rate (even low grade or asymptomatic) was 4.7%, with a 4.7% mesh exposure rate. (Int. Urogyn. J. (2006) 17 (Suppl. 2) S212, Abstract; Int. Urogyn J. (2007) 18:743-752).

By 2008, eight published Prolift studies of 1295 women were included in a review by Feiner. With an average of 30 weeks follow-up, these studies demonstrated a mean objective averaged an 87% success rate and a mean complication rate of 16%. Mesh exposure was reported at 7%, dyspareunia at 2%, vaginal or buttock pain at 2%, and contraction in 1.5%. (Feiner, B. et al., Efficacy and safety of transvaginal mesh kits in the treatment of prolapse of the vaginal apex: a systematic review, BJOG 2009;116:15-24, accepted 2008).

The experience of 3 U.S. centers participating in the initial prospective TVM studies was reported in 2011. (Miller 2011.) This trial (and its French counterpart addressed below) employed a mesh implant made of Gynemesh PS shaped very similarly to the Prolift implant but without the Prolift surgical tools. In this trial of 85 patients, of which 66 were available for

follow up at 5 years, the 5-year success rate, defined as leading edge above the hymen, was found to be 89%. Mesh exposure occurred in 16 out of 85 patients and 6 of those patients had recurrent episodes. Their population had a 30% pre-surgery dyspareunia rate (12 of 40 sexually active patients). In 8 of those 12 patients, dyspareunia resolved after TVM surgery. There were 3 cases of de novo dyspareunia.

The five year follow up on the corresponding TVM study cohort of 90 patients from France was published in 2013, and showed a composite 84% success rate at 5 years, defined as the leading vaginal edge above the hymen, the patient having no bulge symptoms, and no surgical re-intervention for recurrent prolapse. (Jacquetin 2013.) The anatomical success rate was 79% after five years. Fourteen patients experienced mesh exposure over 5 years. New onset dyspareunia was reported in 3 of the sexually active patients (10%) at five years, and one patient reported new onset mild pelvic pain at 5 years. Shorter-term follow up on the TVM patients in France and the US has also been published.

De Landsheere et al. reported retrospectively on 524 consecutive patients who underwent Prolift repair between January 2005 and January 2009, with a median follow-up of 38 months. The re-operation rate for prolapse recurrence was 3% and the rate of intervention for mesh-related complications was 3.6%. Intra-operative complications were limited to 3 cystotomies (0.7%) performed during initial dissection and repaired, and 1 rectal injury (0.2%) performed during initial dissection and repaired. Three patients (0.6%) had post-operative blood loss greater than 400 cc, all of whom required re-operation with either laparotomy or laparoscopy. Of the 19 patients (3.6%) who required intervention for mesh complications, 14 (2.7%) had mesh exposure requiring partial mesh excision. Mesh infection (0.2%), symptomatic mesh retraction (0.4%), rectal compression causing constipation (0.4%) and symptomatic vaginal synechia

(0.4%) were the rarer of the indications for interventions related to mesh complications. The authors found that the three year median follow up demonstrated that Prolift was safe and effective and that rates of complications because of the use of mesh kits and prolapse recurrence were low. (De Landsheere L, et al: Surgical intervention after transvaginal Prolift mesh repair: retrospective single-center study including 524 patients with 3 years' median follow-up. Am. J. Obs. and Gynecol. 2012, 206(83): e1-7.)

Furthermore, a substantial number of randomized controlled trials have assessed Prolift against various forms of native tissue repairs. In 2014, da Silveira et al. published their RCT comparing native tissue repair (site specific repair with sacrospinous fixation) to Prolift in 184 patients with stage 3 or 4 prolapse. 90 patients were in the native tissue group and 94 in the mesh group. 169 women completed one year follow up. There were no significant difference in sexual function scores at baseline and 1 year after surgery. Although mesh exposure was found in 18 patients (20%), only 3 of those patients required reoperation. At the end of one year, anatomic cure rates were significantly superior in the mesh group in the anterior compartment. Greater improvements in quality of life were achieved in the mesh group: "When we analyzed the quality of life scores according to the pQoL, there was a significant improvement in each group and a greater improvement of quality of life in the mesh group. When we observed the superiority of the anatomical cure, it was expected to result in an improved quality of life, which occurred in the group studied even in spite of the high extrusion rates." Although the mesh group had a higher rate of complications, patient satisfaction was high. (da Silveira SRB et al: Multicenter, randomized trial comparing native vaginal tissue repair an synthetic mesh repair for genital prolapse surgical treatment. Int. Urogynecol. J. 2014).

Altman et al. randomized 389 women with anterior prolapse to traditional anterior colporrhaphy (189) or Anterior Prolift (200). The trial was conducted at 53 hospitals throughout Sweden, Norway, Finland and Denmark. The primary outcome was a composite of both objective and subjective criteria. At 1 year, 60.8% in the Prolift group achieved the primary outcome as opposed to 34.5% in the colporrhaphy group. Surgical correction of mesh-exposure occurred in 3.2% of 186 patients in the Prolift group. Furthermore, for the Prolift group, the operative times were longer, symptoms of SUI were more bothersome, the blood loss was higher, and the bladder perforation rate was higher. The authors found an increase in dyspareunia after the use of Prolift as compared with colporrhaphy, "although overall reported satisfaction in sexual life was similar in the two groups." Ultimately, the authors concluded that the "use of a standardized trocar-guided mesh kit resulted in a significantly higher rate of treatment success than did traditional colporrhaphy for repair of anterior wall prolapse." (Altman D, et al: Anterior colpoprrhaphy versus transvaginal mesh for pelvic-organ prolapse. NEJM. 2011, 364(19): 1826-1836).

Withagen M. et al. conducted a multicenter randomized controlled trial of 190 women with *recurrent prolapse* who undergoing either conventional vaginal repair (97 patients) or a mesh-augmented repair with Prolift (93 patients). At one year follow up, anatomic failure in the treated compartment (POP-Q stage 2+) was seen in 45.2% of patients undergoing traditional native tissue repair and in 9.6% of the patients undergoing mesh augmented repair. Six percent of the patients in the mesh group required excision of mesh exposures. Mesh exposure was found in 14 patients (16.9%), of whom 9 were asymptomatic and 5 required intervention. At one year, 11.7% of the native tissue repair group and 10% of the Prolift group had pain in the lower abdomen or in the genital area. Preoperatively, 51% of the native tissue repair group and 56% of

the mesh group were sexually active. At one year, 53% of the native tissue repair group and 57% of the mesh group were sexually active. In both groups, rates of dyspareunia as reported by 10% of the native tissue repair and 8% of the mesh group. De novo pain and de novo dyspareunia rates were low and equally distributed among both groups. The authors noted "significant lower failure rates in the anterior as well as the posterior compartment after tesion free vaginal mesh insertion." In addition, at 1 year, most of the anatomic failures were stage 2 prolapses and not bothersome enough to lead to intervention. (Withagen M, et al: Trocar-guided mesh compared to conventional vaginal repair in recurrent prolapse: a randomized controlled trial. 2011, Obstet Gynecol 117:242-250).

Several other RCTs also demonstrated higher anatomic success with Prolift than with a form of native tissue repair:

- Nguyen et al. randomized 75 patients with anterior vaginal prolapse to colporrhapy (38) versus Anterior Prolift (37). Surgical success one year after surgery was achieved in 87% of the mesh group and in only 55% of the colporrhaphy group. The vaginal mesh extrusion rate was 5%. De novo dyspareunia was reported in 16% of the colporrhaphy group and in 9% of the mesh group. (Nguyen JN: Outcome after anterior vaginal prolapse repair: a randomized controlled trial. Obstet Gynecol 2008:891-8).

- In Halaska's RCT, 168 patients with post-hysterectomy vaginal vault prolapse were randomized to sacrospinous fixation (83) versus Total Prolift (85). At one year, prolapse recurrence was noted in in 39.4% of the sacrospinous fixation group, and in 16.9% of the Total Prolift group. The symptomatic vaginal exposure rate was 5%, and most of these were treated without general anesthesia. (Halaska M et al: A multicenter, randomized, prospective, controlled study comparing sacrospinous fixation and transvaginal mesh in the treatment of posthysterectomy vaginal vault prolapse. Am J obstet Gynecol 2012: 301).

- Svabik et al. randomized 70 patients with posthysterectomy vault prolapse to sacrospinous fixation with native tissue repair (34) versus Total Prolift (36). Anatomic success on clinical examination at the end of one year was achieved in 97% of the Prolift group and only 35% in the sacrospinous fixation group. (Svabik K et al: Comparison of vaginal mesh repair with sacrospinous vaginal colpopexy in the management of vaginal vault prolapse after hysterectomy in patients with levator ani avulsion: a randomized controlled trial. Ultrasound Obstet Gynecol 2014).

Additional studies have reported mean 7-year follow up on Prolift patients. In Meyer et al., 94% of patients at 7 years met anatomic success criteria using the hymen as the threshold. 84.3% reported being somewhat or completely satisfied. The authors reported a long term exposure rate of 6%, and all of the exposures were in patients with significant vaginal atrophy. Dyspareunia was reported in 36% of study population, but the authors noted that the actual de novo dyspareunia rate that was related to mesh was unclear because the baseline rate of dyspareunia was not known. The authors note that dyspareunia is not unique to mesh augmentation, as studies report dyspareunia rates between 19-37% with native tissue repair. They also note (citing Lowman 2008) that, even with dyspareunia, as many as 85% of patients report satisfaction with their surgical results. See also Heinonen 2016, reporting 80.1% patient satisfaction at 7 year follow up.

The Maher Cochrane review issued in 2016 is a highly-regarded systematic review of 37 randomized controlled trials (RCTs), covering 4023 patients, which compared various forms of vaginal prolapse repair (mesh, biological graft, or native tissue). When comparing TVM to native tissue repair, the authors observed that: (1) Native tissue vs. mesh repair awareness of prolapse at one to three years was less likely after mesh repair; (2) Rates of repeat surgery for prolapse were lower in the mesh group; (3) More women in the mesh group required repeat surgery for the combined outcome of prolapse, stress incontinence, or mesh exposure; (4) Recurrent prolapse on examination was less likely after mesh repair; (5) Permanent mesh was associated with higher rates of de novo stress incontinence and bladder injury; and (6). There was no evidence of a difference between the groups in rates of de novo dyspareunia.

Also in 2016, the Society of Gynecologic Surgeons (lead author M. Schimpf) performed its own systematic review of 66 comparative studies, including 38 randomized trials on native

tissue repair versus graft augmentation. In the publication of this review, Schimpf et al. found that in the anterior vaginal compartment, synthetic nonabsorbable mesh consistently showed improved anatomic and bulge symptom outcomes compared with native tissue repairs, but found no difference in anatomic or quality-of-life outcomes following mesh use in the posterior compartment compared with native tissue repair. Subjective outcomes, including urinary incontinence and dyspareunia, generally did not differ between mesh and non-mesh groups. Mesh erosion rates ranged from 1.4 to 19% in the anterior compartment, and 3-36% when mesh was placed in multiple compartments, but reoperation rates were low (3-8%).

X. PROLIFT +M

In 2009, in response to surgeon feedback regarding implant materials, Ethicon introduced Prolift + M to the market. (ETH.59475-59508). This device was identical to Prolift except that the implant was made of Ultrapro, a mesh comprised of both non-absorbable Prolene and absorbable Polyglecaprone-25 monofilament (Monocryl). In addition, the posterior arms were angled a bit differently from the Prolift. After absorption of the Monocryl product, the remaining Prolene was lighter in weight ($31g/m^{2)}$ compared to Gynemesh –PS ($45g/m^2$) without losing the strength of the original product. (Milani et al. 2011).

There are several studies in the published medical literature demonstrating the safety and effectiveness of Prolift +M. Milani et al. presented data on 127 women with stage 3 and higher prolapse who underwent the repair. (Milani et al., Trocar-guided mesh repair of vaginal prolapse using partially absorbable mesh: 1 year outcomes, Am J. Obstet. Gynecol. 2011:204:74.e1-8). This study was sponsored by Ethicon and includes employees of Ethicon as co-authors, reflecting Ethicon's involvement in the dissemination of the study outcomes to

physicians. The three-month results of the study were presented at the 34th Annual Meeting of IUGA in June 2009. 124 patients completed one year follow up. At 1 year follow up, anatomic success (defined as prolapse stage less than/equal to stage 1 in the treated vaginal compartments) was 77.4%. Significant improvements in bother, quality of life and sexual function were noted at 3 months and 1 year as compared with baseline. At 1 year, 86.2% of patients noted that their prolapse was "much better". The mesh exposure rate was 10.2% and the de novo dyspareunia rate was 2% at one year. The authors found that the results of the study suggested anatomic support consistent with the original Prolift mesh.

The three year follow up on the patients in the Milani study was also published. (Milani et al., Medium-Term Clinical Outcomes following trocar-guided mesh repair of vaginal prolapse using partially absorbable mesh; Int. Urogyn. J. (2012) 23 (Suppl 2):S43-S244). At 3 years follow up in 109 of the original patients, anatomical success was 75.9 %. Mesh exposure was observed in 19 subjects over 3 years (14.8 %) and no subjects had de novo pelvic pain. Resolution of pre-existing pelvic pain occurred in 7 (5.5 %) subjects. De novo dyspareunia was observed in 3/33 subjects (9 %), and the causes were vaginal atrophy, uterine prolapse and 1 unknown. Preexisting dyspareunia resolved in 6/18 subjects. The authors concluded that these medium term results demonstrated sustained anatomic and functional results, no major safety concerns were identified, and the "low incidence of pain and dyspareunia are encouraging."

Khandwala (2013) presented 1 year data showing a composite success rate of 88.1%. (Khandwala, S., Transvaginal mesh surgery for pelvic organ prolapse: one-year outcome analysis, Female Pelvic Med. & Recon. Surgery, Vol. 19, No. 2 (March/April 2015). "There were 3 cases (2.2%) of mesh exposure in the vagina. There were no visceral injuries. The

incidence of de novo dyspareunia was 6%."

In 2014, Quenemer et al. reported their series of 250 patients who were followed for a median of 20 months. (Quenemer J. et al., Rate of re-interventions after transvaginal pelvic organ prolapse repair using partially absorbable mesh: 20 months median outcomes; Eur. J. Obstet. & Gynecol. & Reprod. Biol., 175 (2014): 194-98. The rate of re-interventions was 8%. The main indications were mesh exposure (2%), prolapse recurrence (1.2%), and stress urinary incontinence (4.8%). These authors compared their data with what was previously obtained in their center with non- absorbable mesh. The authors concluded that Prolift +M is "reliable and secure", and found comparable among Prolift and Prolift +M rates of re-intervention for mesh-related complications and for recurrence.

Lensen et al. reported on a retrospective cohort trial comparing Prolift and Prolift +M at one year postoperatively. (Lensen EJM et al., Comparison of two trocar-guided trans-vaginal mesh systems for repair of pelvic organ prolapse: a retrospective cohort study, Int'l Urogynecol. J. (2013). The authors found no significant difference between the Prolift and Prolift +M mesh in the primary outcome: composite outcome failure. Of note, the authors found: "Despite the considerable sample size of our study, no clinically relevant difference was demonstrated between the two groups of mesh." Fewer mesh exposures were noted in the Prolift +M group than in the Prolift group (5% vs. 12%). However, the authors noted that "it was impossible to know whether this was mainly due to the mesh properties or the increasing experience of the surgeons or a combination of both. Other complications and patients' overall improvements were similar." No differences were found in functional outcome measures such as urinary incontinence, bulge symptoms pain or dyspareunia. (See also Bhatia N. et al., A comparison of

sexual function outcomes 1 year after undergoing a transvaginal mesh procedure using polypropylene mesh vs. hybrid polypropylene/polglecaprone mesh (oral poster), Female Pelvic Med. & Recons. Surg, March/April 2012). Otto (2013) has suggested based on mechanical testing that the porosity of Prolift +M mesh disappears when tension is mechanically applied to the implant. However, the mechanical testing performed in this study does not hold the weight of the clinical studies discussed above, where the product is implanted in women and assessed in its intended indication, which do not reflect excessive scarring or other indications that the mesh's pores are too small to permit proper tissue integration. Otto's conclusion is also not consistent with my extensive clinical experience implanting and explanting mesh.

My search of the medical literature does not reveal trials demonstrating or concluding that Prolift +M is more effective or safer than Prolift, or vice versa. That is consistent with my personal experience with Prolift +M, as my clinical outcomes with Prolift and Prolift +M were indistinguishable.

The discontinuation of Prolift and Prolift +M in 2012was a significant setback for the surgical treatment of pelvic prolapse. No other procedure offered the unique capabilities or advantages that Prolift did. Currently there are no trocar-based products on the general market. The implants that are available do not allow for dynamic tensioning of the implant, are more invasive to place, and are less secure.

XI. PUBLIC STATEMENTS BY THE FDA ON THE USE OF TRANSVAGINAL MESH TO TREAT PROLAPSE.

On October 20, 2008, the FDA issued a public notification informing surgeons that it had received over 1000 complaints alleging complications following the use of surgical mesh to treat either prolapse or SUI. The FDA did not specify how many complaints were specific to prolapse treatment and did not identify any particular brand of product. Over the next few years, the FDA conducted a review of complaints submitted to the agency and a systematic review of medical literature assessing prolapse and SUI meshes.

In July 2011, it issued an updated public notification that was specific to transvaginal mesh to treat prolapse but specifically excluded an analysis of slings to treat SUI.

In September 2011, the FDA convened an Advisory Panel to hold two days of hearings on the evidence surrounding the use of mesh transvaginally to treat prolapse and SUI. In 2014, the FDA issued proposed rules to move transvaginal prolapse kits such as Prolift and Prolift +M from Class 2 to Class 3 devices which would require premarket approval rather than 510k clearance. Those proposed rules became final in 2016. However, at that time, Prolift and Prolift +M were already discontinued and Ethicon had previously revised the indications for Gynemesh PS for abdominal-only indication.

XII. MATERIAL PROPERTIES OF THE MESH

Many of plaintiffs' expert witnesses have suggested that the Gynemesh PS mesh that comprises Prolift is not suitable to treat prolapse transvaginally. In particular they claim that the mesh degrades, is cytotoxic, that its pore size is too small, that the mesh contracts, ropes and

curls and that it causes a chronic foreign body reaction that is harmful to patients. I disagree with these arguments and have concluded that the mesh is safe and effective material for this use.

The non-absorbable polypropylene used in Gynemesh PS, Prolift and Prolift +M is knitted from filaments of Prolene, Ethicon's branded recipe of polypropylene. The use of Prolene as an implant in the human body, both as a mesh and as a suture, goes back decades. Prolene sutures have been utilized for decades in surgery throughout the body, including in cardiac surgery. Prolene meshes have been utilized to repair hernias since the 1970s, now 40 years. Starting with the 1996 publication of patients by Prof. Ulmsten and Nilsson, we now have over 20 years of published literature from surgeons throughout the world tracking their performance of Prolene used in transvaginal indications (although the mesh used in TVT is a different knit construction than Gynemesh PS, and the Prolift products). That data has been published at every level of study but most importantly in RCTs and systematic reviews and metananalyses – the highest levels of evidence. (Oxford Pyramid).

The mesh used in Gynemesh PS and the Prolift products is macroporous, Type 1 mesh under the Amid classification. Under that classification system, meshes with pore sizes over 75 microns are macroporous. (Amid 1997). The pore size of Gynemesh PS is 2.44 mm/2440 microns far in excess of that. (Jones et al., Int'l Urogyn J. 2009; 20:847-53). The pore size of the Ultrapro mesh used in Prolift +M is 2.5 mm prior to incorporation of the Monocryl and 3.5 mm following incorporation. (Lensen 2013).

There is no credible body of evidence in the published medical literature that demonstrates that meshes knitted of Prolene filaments degrade after implantation in any way that manifests clinically for patients. That conclusion is inconsistent with the numerous TVT studies

discussed above reporting high success rates even at follow up of ten years or more (these studies are discussed in my general TVT product expert report and are incorporated here by reference). Polymer scientists Thames et al. cleaned explanted Prolene and found that "Our effective cleaning of explanted Prolene meshes and subsequent analyses showed that they did not degrade in vivo. Instead, the cracked layer that some researchers have identified as degraded Prolene is an adsorbed protein-formaldehyde coating, resulting from the well-established formalin-protein fixation process that occurs immediately upon placing an explant in formalin." (Thames, SF et al., Int'l Urogyn. J. 2016). In the responses to Frequently Asked Questions published jointly by AUGS and SUFU in 2014, those two organizations specifically pointed to the long history of the use of polypropylene as midurethral slings in rejecting the notion that any 'surface-cracking' on polypropylene has a clinical impact on patients. (AUGS/SUFU Frequently Asked Questions to Providers, Mid-urethral slings for SUI, March 12, 2014). In Woodruff's histopathologic analysis on 24 explants (polypropylene, autologous fascia, porcine dermis, cadaveric dermis and cadaveric fascia) at 2-34 months after implantation, no graft degradation had occurred in the polypropylene material. (Woodruff AJ et al., Urology 2008).

In support of their degradation theories, Plaintiffs' experts often rely upon the study published by Henri Clave et al., which reported on explanted mesh implants from women with mesh erosion and/or 'infection' after mesh augmented reconstructions in comparison to a control group of new mesh implants. However, this single study cannot be the basis for a conclusion that mesh knitted from Prolene degrades in the body, not only because of the small study population, but also because the study does not examine meshes implanted in women who are not experiencing complications. Even the study authors acknowledge that the oxidation of polypropylene "can neither be confirmed nor excluded' in the in-vivo environment" and

"prediction of normal in-vivo sling material aging or the range of consequences in the clinical state beyond the observed samples is not possible. Due to small effective sample size, it is not possible to categorically conclude on the basis of statistical analysis even if a clear tendency is present." (Clave H. et al., Int. Urogyn. J. 2010).

I have explanted mesh on a number of patients. Most of these patients have been referred to my practice from outside sources. At the time of surgery, I have never seen any evidence of degradation of polypropylene mesh. Usually, the mesh is nicely incorporated into the tissues. I have seen evidence of chronic inflammation associated with mesh erosion and/or extrusion. However, the mesh itself has never shown any evidence of degradation.

Plaintiffs' experts also suggest that the contraction of the mesh is an inherent defect of the implant material that causes severe and prolonged pain and other complications. First, the mesh itself does not contract. The notion that it does is contradicted by the clinical observation that initial cure rates tend to decline over time. If the mesh were to contract or shrink excessively in all patients due to its intrinsic material properties, this would not be the case.

Certainly, it is a known and expected phenomenon of wound healing that when the mesh is implanted, there is a normal scar tissue that forms, as with any surgery. Scars can be associated with wound contraction, and in a small proportion of patients, this can result in pain. This is a risk of wound healing that exists whether or not mesh is used. This is reflected the equivalent dyspareunia rates that are reported in reputable studies comparing mesh and non-mesh prolapse repairs (Maher C. Cochrane Review (2016); Schimpf, M. SGS Systematic Review (2016); Dietz V. & Maher C., Pelvic organ prolapse and sexual function, Int. Urogyn. J. (2013) 24:1853-57; Niemimen K. et al., Symptom resolution and sexual function after anterior vaginal

wall repair with or without polypropylene mesh, Int. Urogyn. J. (2008) 19:611-1616; (Svabik et al, Comparison of vaginal mesh repair with sacrospinous vaginal colpopexy in the management of vaginal vault prolapse after hysterectomy in patients with levator ani avulsion: a randomized controlled trial, Ultrasound Obstet Gynecol 2014 Apr, 43(4):365-71).

The IFUs for Prolift have always warned of the potential risk of scarring associated with contraction and also instruct doctors to implant the mesh loosely. Moreover, the Prolift Surgeon's Resource Monograph notes that "The collagen-dominant layer that invests the mesh will contract over time and cause an estimated 10-20% contraction. This is why it is important to avoid excessive mesh trimming intraoperatively." (ETH.MESH.03460818).

Finally, Plaintiffs' experts portray the chronic foreign body reaction that ensues following implantation of Gynemesh PS and the Prolift products as a severe adverse event resulting in long-lasting and severe complications. That is not the case. If it were the case, chronic pain would be reported in randomized controlled trials more frequently with Prolift than with native tissue repairs, but that is not the case. (See, for example, Withagen 2011, Altman 2011, da Silveira 2014).

When the mesh is first implanted, this generates an acute inflammatory process that, after a period of time, evolves into the body's normal process of integrating the implant into the body's tissues. This is not an adverse event, it is an expected histological process (as it is with other implanted foreign bodies, such as breast implants). While I am not a histologist or pathologist, neither my review of the medical literature nor my extensive experience implanting slings and providing post-operative treatment supports the notion that the chronic foreign body reaction generates severe complications for patients.

XIII. COMPLICATIONS

There is a known body of potential risks or adverse events that are common to all forms of surgical treatment of prolapse, and transvaginal mesh is no exception. These include urinary symptoms such as incontinence, urinary retention, voiding dysfunction, urinary tract infection, overactive bladder symptoms (include frequency, urgency and urge incontinence), as well as tissue and organ damage, nerve damage, hematoma, wound complications, excessive scarring, vaginal pain, pelvic pain and pain with sexual intercourse. These risks of prolapse surgery are widely known by surgeons based on their training and based on the fact that they are reported in the published medical literature. As noted in the ACOG Committee Opinion No. 513 (Dec. 2011), "like repairs augmented with mesh, native tissue repairs also may be associated with complications, including pain, dyspareunia, granulation tissue formation, and recurrences, all of which may require subsequent intervention." Mesh exposure, extrusion and erosion is the only risk of prolapse surgery that is unique to mesh.

Mesh exposure and erosion

Mesh exposure and erosion are known risks of transvaginal mesh surgery. Most often, mesh exposure into the vaginal wall is what is observed. It can be symptomatic or asymptomatic. When it does not bother the patient or her partner, it can be left untreated or treated with estrogen cream. Otherwise the mesh can be revised in an in-office procedure, or where necessary, in the operating room. Occurrence rates of mesh exposure are typically under 18%, as reported in the studies discussed in detail above, and are impacted on an individual level by various factors such as concomitant hysterectomy, patient age, wound healing factors and the implanting surgeon's experience level. (Kelly EC et al., Surgeon experience and complications

of transvaginal prolapse mesh, Obstet. Gynecol. 2016). Systematic reviews of complications, such as Diwadkhar 2009 and Abed 2011, have cited erosion rates of 5.8% and 10.3%, respectively. de Landsheere et al, who reported 3 year median follow up on a study of 524 Prolift patients, reported that 19 patients (3.6%) presented with mesh-related complications with a reoperation rate for mesh exposure of 2.5%. Benbouzid studied Prolift in a cohort of patients with 4.5 years follow up and found no recurrence leading to reoperation and an 85% cure rate defined as POP-Q Stage 0-1. (Benbouzid 2012). No recurrences were beyond POP-Q Stage II and mesh exposure occurred in four patients (5.3%), with two undergoing revision and two successfully treated with estrogen. By way of comparison, Benbouzid observed that the long-term studies published about sacrocolpopexy reported significant mesh exposure between 6 and 9%. (Ross JW & Preston M. Laparoscopic sacrocolpopexy for severe vaginal vault prolapse: five-year outcome. J. Minim. Invasive Gynecol. 2005; 12:221–6; Higgs PJ, et al. Long term review of laparoscopic sacrocolpopexy. BJOG 2005; 112:1134–8). This literature is consistent with the Ethicon's Prolift Surgeon's Resource Monograph, which cites exposure rates between 3 and 17%.

While the literature typically reflects a lower mesh exposure rate for abdominal sacral colpopexy, the Nygaard 2013 analysis of seven year follow up on sacral colpopexies performed in the original CARE trial estimates a 10% exposure rate at 7 years. (Nygaard JAMA study (2013); ACOG-AUGS Practice Bulletin No. 176 (April 2017)).

There are patient characteristics which may increase the risk for mesh exposure. Clearly, there are some chronic medical conditions that interfere with wound healing and may make exposure rates more likely, such as diabetes. In addition, patients who fail to adhere to their

vaginal restrictions in the immediate postoperative period are clearly more at risk for mesh erosions.

Erosion of the mesh into surrounding organs such as the bladder or urethra is very infrequent but can result in serious symptoms requiring prompt attention and likely a more complex surgical intervention.

Dyspareunia

Dyspareunia or pain with intercourse is an established risk of any vaginal surgery, and transvaginal mesh implantation is no exception. This is also true of hysterectomy, which is sometimes performed concomitantly with prolapse surgeries. (Abdelmonen 2010). Notably, however, numerous studies have found no overall difference in incidence of post-operative dyspareunia, sexual functioning by PISQ scores, change in total vaginal length and change in vaginal caliber between prolapse surgery with Gynemesh PS or Prolift and surgery without mesh. (Carey 2007; Withagen 2011; Altman 2011; Sokol 2012; Halaska 2012; El-Nazer 2012; Svabik 2014; daSilveira 2014). This has also been noted in published studies and meta-analyses assessing the use of mesh vs. native tissue repairs more broadly. (Dietz & Maher, Pelvic organ prolapse and sexual function, Int. Urogyn. J. (2013) 24:1853-1857; Maher Cochrane Review (2016).

These findings are consistent with the study by Lowman (2008) who compared dyspareunia findings with Prolift specifically to studies analyzing other prolapse procedures. Lowman found no increased risk of de novo dyspareunia with Prolift (16.7%) as compared with other types of prolapse procedures that do not incorporate vaginal mesh, such as USLS, SSLF, colporrhaphy and sacral colpopexy (range 14.5 – 36.1%). (Lowman 2008 Importantly, although

16.7% of patients developed de novo dyspareunia following Prolift, 85% of patients were satisfied with their results and would have the surgery done again: "patient's willingness to have this surgery again supports the fact that the presence or absence of dyspareunia, although significant, does not determine a woman's overall sexual health."

Pain with intercourse after posterior native tissue repair, or posterior colporrhaphy is a particularly significant risk. Francis and Jeffcoate (J. Obst. & Gyn. 1961) attributed a 50% rate of dyspareunia to this procedure. Kahn and Stanton in 1997 reported that: "Dyspareunia is a "major post-operative complication" of posterior colporrhaphy; "This retrospective study shows that posterior colporrhaphy is associated with an increase in bowel and sexual dysfunction." (Kahn MA et al., Posterior colporrhaphy: its effects on bowel and sexual function, BJOG (1997) 82-86). Over the years, surgeons have developed techniques to decrease the rate by not overtightening the introitus, not performing levatoplasty or performing a "site specific" technique, but even with these changes, authors have reported a 16-17% rate of dyspareunia following posterior repair and perineonorraphy. (Abramov, Y., Site-specific rectocele repair compared with standard posterior colporrhaphy, Obstet. Gynecol. (2005 Feb); 105(2):314-8). Weber A. et al. (2000) reported de novo dyspareunia was 26% (14/53) following posterior colporrhaphy, and 38% (8/21) for those who had both Burch and posterior colporrhaphy.

Pelvic pain

The etiology of pelvic pain following placement of mesh is often complicated, multi-factorial, and difficult to ascertain. Even among women who have not had mesh implants, chronic pelvic pain is not rare. It can be a vexing condition to treat and often has multiple etiologies. Objective disease state such as endometriosis, pelvic adhesive disease, uterine

fibroids, adenomyosis and ovarian cysts have also been associated with chronic pain. Urogenital atrophy is a virtually universal condition in postmenopausal women. It is typically associated with chronic pain and dyspareunia. Obstetrical injury and/or lacerations can also lead to vaginal deformities, vaginal scar tissue and chronic pain. There are also psychosocial issues, such as a history of sexual abuse, which can be associated with chronic pain and dyspareunia. Spasms of the pelvic floor muscles can lead to vaginismus and chronic pain. Multiple vulvar conditions including lichen sclerosis and chronic vulvitis can lead to persistent discomfort. All of these conditions are more common than surgically associated discomfort. This list is not meant to be inclusive or complete.

Commonly known risks of surgery

Besides that knowledge which is gleaned from surgical training and experience, the published medical literature over the years demonstrates long-held knowledge within the medical community regarding the potential risks of mesh surgery.

The risk of mesh erosion has been documented in the publicly available medical literature for decades, as demonstrated by these examples:

- In 1997, Iglesia C. et al. discussed certain "[d]isadvantages of synthetic mesh…include[ing] foreign-body reaction with the risk of infection, rejection and erosion." Iglesia, CB et al., The Use of mesh in Gynecologic Surgery, Int'l. Urogyn. J. 1997;8:105-115.

- In 2003, Dietz HP wrote that "Synthetic suburethral slings have become popular despite the risk of erosion commonly associated with synthetic implants." Dietz, H.P. et al., Mechanical properties of urogynecologic implant materials, Int'l Urogyn. J. (2003) 14:239-243.

- In 2006, Boulanger et al. wrote: "These synthetic meshes are all associated with specific complications, especially erosion." Boulanger L., et al., Tissue Integration and tolerance to meshes used in gynecologic surgery: An experimental study, Eur. J. Obstet. Gynecol. Reprod. Biol 2006; 125:103-108.

- Choe J.M. et al reported that "Infectious and erosive complications of synthetic materials are well-known." Choe, J.M. et al., The use of Synthetic materials in pubovaginal sling, Adv. Exp. Med. Biol. 539 (Part A):481-92 (2003).

Pain with intercourse and sexual dysfunction has also been documented in publicly available literature for decades as a potential risk of vaginal surgery. For example:

- As early as 1961, Francis W et al. reported: "Apareunia and dyspareunia are well-accepted complications of operations which involve incision and suture of the vagina." Francis, Winifred J.A., et al., Dyspareunia following vaginal operations, Journal of Obstet. & Gynecol of the Brit. Commonwealth (Feb 1961) Vol LXVIII, No. 1:1-10.

- In 2002, Maaita et al. reported:"Dyspareunia is a well-accepted complication of operations which involve incision and suture of the vagina. Surgeons should aim to improve sexual function in women after surgery for urinary stress incontinence, particularly in those with incontinence during intercourse. However, vaginal surgery may be detrimental to sexual activity afterwards because of narrowing or scarring, tape/sling erosion, and vaginal discharge, the tape inserted too tightly, failure of the technique resulting in persistent leak during intercourse, and psychological problems linked with surgery, e.g., fear that intercourse will damage the surgical result." Maaita, M. et al., Sexual function after using tension free vaginal tape for the surgical treatment of genuine stress incontinence", BJU International (2002) 90:540-543.

- In 2005, Shah SM et al. wrote: "Although the use of synthetic materials such as polypropylene appears to be safe and effective in the treatment of SUI, concern exists that the presence of the material in the vagina might adversely affect sexual function." Shah SM et al., Impact of vaginal surgery for stress urinary incontinence on female sexual function; is the use of polypropylene mesh detrimental? Urology (2005) Feb; 65(2) 270-4.

XIV. ALTERNATIVE SAFER DESIGN

I am not aware – either based on my experience or my review of the medical literature- of an alternative material or alternative design to the Prolift devices that reduces or eliminates their potential risks. Some experts claim Prolift +M is a safer alternative to Prolift. However, the published literature discussed above does not support their assertions.

XV. PRODUCT WARNINGS

I have reviewed the IFUs for Gynemesh PS and the Prolift products, as well as professional education materials such as the Prolift Surgical Technique Guide and the Prolift Surgeon's Resource Monograph. It is my opinion that these documents accurately warn of the potential risks of the use of these slings as they are reported in the highest levels of medical literature which I have reviewed. They also appropriately take into consideration the risks that are commonly reported and known to trained pelvic floor surgeons who are the intended users of these devices.

My opinion is based on the following sources:

1. Several years of published medical literature on transvaginal mesh to treat prolapse including Prolift. This includes Level 1 meta-analyses, systematic reviews, and randomized controlled trials, as well as numerous prospective studies.

2. I have also reviewed and considered the FDA's "Blue Book Memo" which provides guidance on device labeling, and Ethicon's Standard Operating Procedure on Labeling (HMESH_ETH_11642462). These sources are informative, but do not weigh as heavily as the medical literature that assess the performance of these devices in thousands of women over years.

3. My training in urogynecology and pelvic reconstructive surgery as a resident.

4. My surgical experience in implanting slings and mesh to treat prolapse over the past 17 years and managing those patients' post-operative care, as well as treating patients who were implanted with mesh by other doctors.

5. My years of experience in training residents, fellows and physicians in how to perform sling procedures. I have also been in involved in postgraduate training sessions and

cadaver labs which are focused on the indications, techniques, and complications of mid urethral slings.

6. My attendance at numerous local and national medical conferences, including the Annual Meetings of medical societies such American College of Obstetrics/Gynecology. I have also participated in annual conferences of the American Association of Gynecologic Laparoscopists. At these meetings, I have observed numerous presentations regarding clinical studies of transvaginal mesh by surgeons who have presented their findings, as well as with my informal interactions with my colleagues.

The Prolift IFU appropriately takes into consideration the body of surgical knowledge common to trained pelvic floor surgeons and informs surgeons that the manufacturer expects that they be properly experienced in such procedures. Specifically, the Prolift IFU Warnings and Precautions section provides that "Users should be familiar with surgical procedures and techniques involving pelvic floor repair and non-absorbable meshes before employing the Gynecare Prolift Pelvic Floor Repair System." (ETH.MESH.02341527). This section further advises physicians to avoid large vessels, nerves, bladder and bowel, and that "attention to patient anatomy and correct use of the device will minimize risks." It also reinforces the instructions for the surgical placement of the device in emphasizing: "Avoid placing excessive tension on the mesh implant during handling."

The Adverse Reactions section of the original Prolift IFUs correctly reflects the potential complications that are reported in the most reliable medical literature that are discussed in detail above in my report. Those listed risks include injuries to organs, nerves and vessels associated with the implant surgery, infection potentiation, extrusion, erosion and scarring that results in contraction. The Adverse Reaction section does not list – nor does it need to list – every possible

risk of performing surgery in the pelvic floor. Surgeons do not look to an IFU to replace their professional training regarding risks of surgery. The IFU, while informative and helpful in describing the device and the steps for the device's implantation, is not a substitute for a surgeon's training, experience, judgment and continued education. Furthermore, in light of the volume of published literature in the public domain regarding the performance of these devices, some of it sponsored or supported by Ethicon, it would be inaccurate to suggest that a product's IFU holds the key to a surgeon's comprehensive understanding of potential surgical risks. That is simply not consistent with the realities of medical practice.

I have reviewed the 2009 revisions to the Prolift IFU and the Prolift +M IFU. While these versions use additional language to describe potential risks, they did not provide information that was new to the medical community. The added language either referenced general risks of pelvic floor surgery that are not a function of the device, risks that were previously reported in the published literature, or that are commonly known to a trained pelvic floor surgeon. For example, the references to pelvic pain, pain with intercourse and voiding dysfunction that were added to the Prolift IFU in 2009, are general risks of pelvic surgery, are reported in the published medical literature, and for both of those reasons, are commonly known by trained surgeons. The Prolift professional education slide deck from 2007 also specifically address these complications, including reference to complications rates in the studies available at that time. These risks were specifically listed in the Prolift +M IFU at all times that it was marketed.

The medical literature that I have reviewed and my surgical experience does not demonstrate the cytotoxicity, degradation, and chronic inflammation leading to complications and other negative consequences that plaintiffs' experts claim. For that reason, they do not need

to be included in the IFUs. While a "chronic foreign body reaction" may take place on a histological level for every implant, the medical literature on Prolift does not reflect that this process amounts to an "Adverse Event" with clinical implications for the patient.

The Prolift Surgeon's Resource Monograph, copy approved for use in April 2007, provides detailed information that supplements that provided in the product IFUs. The Monograph presents the best practices collected by a panel of surgeons who were very experienced in Prolift at that time. Much of the information in the Monograph was culled form a series of user forums held in several cities in the US, Europe and Australia. It provided detailed advice on patient selection and preparation, surgical technique, anesthesia and hydrodissection, incisions, sutures, mesh handling, technique pearls, concomitant procedures, postoperative care and potential complications. It also attached a clinical data summary and the Prolift Surgical Technique Guide. In addition, it provides several pages of detailed discussion of potential complications, including hemorrhage, visceral injury, infection, mesh erosion/exposure/ extrusion, dyspareunia and vaginal pain. (ETH.MESH.03460813-53).

Finally, I have reviewed Ethicon's patient brochures for the Prolift products . They appropriately perform the function that is intended for a patient brochure. They discuss the medical condition of prolapse, treatment options and potential risks. The risk discussion mirrors the IFU and is not misleading. While the brochure does not list every risk of surgery, that is not its purpose. Rather, it is the responsibility of the physician to have a comprehensive risk discussion with the patient that is tailored to the patient's individual needs.

XVI. SUMMARY OF OPINIONS

My opinions set forth in this report are made to a reasonable degree of medical certainty. My opinions are based on information and knowledge that I have acquired from my research and review of peer-reviewed medical literature, my education, training, personal experience in private practice, teaching, and discussion and interaction with other pelvic surgeons in professional activities and conferences. I reserve the right to modify or amend my opinions as I review more information.

1. Gynecare Gynemesh PS, Prolift and Prolift +M are safe and effective and supported by a substantial amount of peer reviewed medical literature. This includes the highest levels of evidence, including systematic reviews, meta-analyses and randomized controlled trials.

2. The benefits of these products far outweigh their risks in properly selected surgical candidates. Based on their performance in thousands of women as reflected in the medical literature, as well as my experience, they are not defectively designed.

3. The meshes that are used in these products are safe to use in this indication. Polypropylene, as a mesh and as suture, has been used an implant for decades. The pore sizes are appropriate for proper tissue integration. Nor do these meshes typically result in infection. Based on my review of the medical literature and my experience, the mesh in Prolift +M does not generate an inflammatory reaction that is prolonged or results in more complications than Prolift or Gynemesh PS.

4. The overall body of published clinical evidence (and my experience) does not demonstrate that the PROLENE® filaments from which these products are knitted degrade in a way that is clinically significant to patients.

5. A chronic foreign body response is not an adverse event. It is an expected and desired result of the placement of any surgical implant which reflects the human body's histological process of incorporating a foreign body. The peer reviewed medical literature I have reviewed does not demonstrate that this process generates adverse clinical outcomes when the mesh is implanted according to correct technique.

6. There is no reliable evidence in the published medical literature of an alternative design to these products that either reduces or eliminates their potential risks.

8. The possible risks of Gynemesh PS and the Prolift products are appropriately described in their Instructions for Use, the patient brochures for the Prolift products, and in Ethicon's professional education materials. These materials properly reflect the risks that are reported in the high-level medical literature and appropriately account for the common knowledge of trained specialists.

Expert Rates

My work on this matter has been or will be billed as follows: $350 per hour for records review, preparation of expert reports, and consultation; $2500 per half day of deposition or trial testimony; and $5000 for full day of deposition or trial testimony.

Dated: August 16, 2017